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The European ADHD Guidelines Group replies:



Dr. Micoulaud-Franchi *et al.* raise concerns relating to our 2016 meta-analysis¹ of neurofeedback as a treatment for attention-deficit/hyperactivity disorder (ADHD). It is encouraging that Dr. Micoulaud-Franchi *et al.* agree with us that there is “an urgent need to conduct future research that associates both high quality of [randomized controlled trial] RCT and high quality of [electroencephalography] EEG-neurofeedback sessions.” Consistent with this, we wrote, “Future efforts should focus on implementing standard neurofeedback protocols, ensuring learning, and optimizing clinically relevant transfer.”^{1(p444)} This is in line with the significant advantage for neurofeedback demonstrated in our additional preliminary analysis of the few studies meeting such standards.

Dr. Micoulaud-Franchi *et al.* are primarily concerned about the discrepancy between Cortese *et al.*¹ and a previous meta-analysis (Micoulaud-Franchi *et al.*²), which they argue is surprising, because, in their view, the 2 meta-analyses were essentially based on the same core methodology and the same trials. In response, we would like to make the following points.

1. Do Micoulaud-Franchi *et al.*² and Cortese *et al.*¹ reach different conclusions? The findings of the 2 meta-analyses are substantially similar. Neurofeedback was reported as superior for all most proximal outcomes but not for probably blinded total ADHD or hyperactive impulsive symptoms. The only way the 2 articles differed statistically was that Micoulaud-Franchi *et al.*² found greater neurofeedback efficacy for probably blinded measures of inattention, whereas Cortese *et al.*¹ did not.
2. Did Micoulaud-Franchi *et al.*² and Cortese *et al.*¹ use the same methodology and include the same trials? Micoulaud-Franchi *et al.*² claim that the 2 meta-analyses had the same

methodology. Indeed, the 2 meta-analyses adopted the distinction between probably blinded and most proximal outcomes, first introduced in our 2012 protocol (European ADHD Guidelines Group, PROSPERO CRD42011001393) as a way to deal with the thorny issue of non-blinding of outcomes in nonpharmacologic treatment trials.³ Leaving this aside, however, Micoulaud-Franchi *et al.*² and Cortese *et al.*¹ had different trial inclusion criteria. This explains why Micoulaud-Franchi *et al.*² included 5 trials, whereas Cortese *et al.*¹ included 13. First, in Cortese *et al.*¹, extending our original 2012 protocol,³ we removed the mandatory requirement for studies to have ADHD symptoms-related outcomes. Second, Micoulaud-Franchi *et al.*² excluded studies in which “treatment as usual” or waitlist was the control, which Cortese *et al.*¹ did not. Third, Cortese *et al.*¹ allowed studies in which participants met validated cutoffs on standard ADHD scales to be included, whereas Micoulaud-Franchi *et al.*² included studies only if participants had a full ADHD diagnosis. Furthermore, Cortese *et al.*¹ also included data from the 2015 report by Bink *et al.*⁴ and obtained additional unpublished data from Christiansen *et al.*,⁵ which extended a preliminary report published in 2013. These data were not available to Micoulaud-Franchi *et al.*²

3. Did Cortese *et al.*¹ make correct selections of probably blinded measures? Micoulaud-Franchi *et al.* see the choice of the Behavioral Observation of Students in Schools (BOSS) observational measure as the best probably blinded outcome from Steiner *et al.*⁶ as a mistake. This choice was, in fact, dictated by our protocol, in which direct observation by trained, blinded raters trump adult-rated measures (whether parent or teacher). This rule was introduced to remove, wherever possible, the practically inevitable confound between teacher versus parent ratings and situation (home versus school), because direct observation is not tied to a particular setting. Furthermore, although Micoulaud-Franchi *et al.* are concerned that the BOSS was not completed by blinded raters, Steiner *et al.*⁶ stated explicitly that it was (page 20). In this case, the BOSS was without doubt superior to teacher ratings as a probably blinded measure, because the latter were almost certainly aware of treatment allocation. The other option is to remove the study by Steiner *et al.*⁶ from the “probably blinded” analysis. Doing this retrospectively did not change the results regarding inattention (standard mean difference 0.22, 95% CI -0.04-0.47).

Taking points 2 and 3 together, we would argue that the differences between Cortese *et al.*¹ and Micoulaud-Franchi *et al.*² are due to a combination of different rules for trial inclusion and probably blinded outcome selection.

Micoulaud-Franchi *et al.* also suggest that we should have removed the study by Arnold *et al.*,⁷ which they consider flawed in a number of ways, although according to our assessment using the Cochrane approach, the risk of bias was uncertain or low. In a sense, we have already addressed this point through our sensitivity analysis excluding randomized controlled trials that used what we deemed

nonstandard neurofeedback approaches (including Arnold *et al.*⁷) that produced more promising, albeit more tentative, results. We also ran a sensitivity analysis removing only the study by Arnold *et al.* This did not affect the results (data available on request).

In sum, it goes without saying that neither the Micoulaud-Franchi *et al.*² nor our meta-analysis should be seen as definitive—rather, it provides a stimulus for therapeutic innovation and improvement and better-quality trials.

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